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# Ibuprofen

## Drug Information Provided by Lexi-Comp

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### Special Alerts

#### McNeil Consumer Healthcare OTC Products: Voluntary Recall - January 2010

McNeil Consumer Healthcare has expanded a previous recall to include specific lots of certain additional OTC products. For information on returning the recalled products, contact McNeil Consumer Healthcare at (800) 222-6036.

For additional information and a link to the full list of recalled products and lot numbers, please refer to <http://www.fda.gov/Safety/Recalls/ucm197746.htm>.

#### Ibuprofen: Unapproved Topical Products - August 2009

The U.S. Food and Drug Administration (FDA) issued information for healthcare providers and consumers regarding unapproved topical combination products containing ibuprofen. Unlike oral ibuprofen products (which are FDA-approved), topical products containing ibuprofen are not FDA-approved. Safety claims for topical products containing ibuprofen have not been reviewed by the FDA.

For information, including a list of the unapproved products, please refer to: <http://www.fda.gov/Safety/MedWatch/SafetyInformation/SafetyAlertsforHumanMedicalProducts/ucm179925.htm>

#### ALERT: U.S. Boxed Warning

The FDA-approved labeling includes a boxed warning. See Warnings/Precautions section for a concise summary of this information. For verbatim wording of the boxed warning, consult the product labeling or [www.fda.gov](http://www.fda.gov).

#### Medication Safety Issues

Sound-alike/look-alike issues:

Haltran® may be confused with Halfprin®

Motrin® may be confused with Neurontin®

**Injectable formulations:** Both ibuprofen and ibuprofen lysine are available for parenteral use. Ibuprofen lysine is **only** indicated for closure of a clinically-significant patent ductus arteriosus.



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**Pronunciation**

(eye byoo PROE fen)

**U.S. Brand Names**

- Addaprin [OTC]
- Advil® Children's [OTC]
- Advil® Infants' [OTC]
- Advil® Migraine [OTC]
- Advil® [OTC]
- Caldolor™
- Genpri® [OTC] [DSC]
- I-Prin [OTC]
- Ibu-200 [OTC]
- Ibu®
- Midol® Cramp and Body Aches [OTC]
- Motrin® Children's [OTC]
- Motrin® IB [OTC]
- Motrin® Infants' [OTC]
- Motrin® Junior [OTC]
- NeoProfen®
- Proprinal [OTC]
- Ultraprin [OTC]

**Index Terms**

- *p*-Isobutylhydratropic Acid
- Ibuprofen Lysine

**Generic Available**

Yes: Caplet, suspension, tablet

**Canadian Brand Names**

- Advil®
- Apo-Ibuprofen®
- Motrin® (Children's)
- Motrin® IB
- Novo-Profen
- Nu-Ibuprofen

**Pharmacologic Category**

- Nonsteroidal Anti-inflammatory Drug (NSAID), Oral
- Nonsteroidal Anti-inflammatory Drug (NSAID), Parenteral

**Use: Labeled Indications**

Oral: Inflammatory diseases and rheumatoid disorders including juvenile rheumatoid arthritis, mild-to-moderate pain, fever, dysmenorrhea, osteoarthritis

Ibuprofen injection (Caldolor™): Management of mild-to-moderate pain; management moderate-to-severe pain when used concurrently with an opioid analgesic; reduction of fever

Ibuprofen lysine injection (NeoProfen®): To induce closure of a clinically-significant patent ductus arteriosus (PDA) in premature infants weighing between 500-1500 g and who are ?32 weeks gestational age (GA) when usual treatments are ineffective

**Use: Dental**

Management of pain and swelling

**Use: Unlabeled/Investigational**

Cystic fibrosis, gout, ankylosing spondylitis, acute migraine headache

**Pregnancy Risk Factor**

C/D ?30 weeks gestation

**Pregnancy Considerations**

Adverse events were not observed in the initial animal reproduction studies; therefore, the manufacturer classifies ibuprofen as pregnancy category C (category D: ?30 weeks gestation). NSAID exposure during the first trimester is not strongly associated with congenital malformations; however, cardiovascular anomalies and cleft palate have been observed following NSAID exposure in some studies. The use of a NSAID close to conception may be associated with an increased risk of miscarriage. Nonteratogenic effects have been observed following NSAID administration during the third trimester including: Myocardial degenerative changes, prenatal constriction of the ductus arteriosus, fetal tricuspid regurgitation, failure of the ductus arteriosus to close postnatally; renal dysfunction or failure, oligohydramnios; gastrointestinal bleeding or perforation, increased risk of necrotizing enterocolitis; intracranial bleeding (including intraventricular hemorrhage), platelet dysfunction with resultant bleeding; pulmonary hypertension. Because they may cause premature closure of the ductus arteriosus, use of NSAIDs late in pregnancy should be avoided (use after 31 or 32 weeks gestation is not recommended by some clinicians). Product labeling for Caldolor™ specifically notes that use at ?30 weeks gestation should be avoided and therefore classifies ibuprofen as pregnancy category D at this time. The chronic use of NSAIDs in women of reproductive age may be associated with infertility that is reversible upon discontinuation of the medication. A registry is available for pregnant women exposed to autoimmune medications including ibuprofen. For additional information contact the Organization of Teratology Information Specialists, OTIS Autoimmune Diseases Study, at 877-311-8972.

**Lactation**

Enters breast milk/not recommended (AAP rates "compatible")

**Breast-Feeding Considerations**

Based on limited data, only very small amounts of ibuprofen are excreted into breast milk. Adverse events have not been reported in nursing infants. The AAP considers ibuprofen to be "usually compatible with breast-feeding." Because there is a potential for adverse events to occur in nursing infants, the manufacturer does not recommend the use of ibuprofen while breast-feeding. Use with caution in nursing women with hypertensive disorders of pregnancy or pre-existing renal disease.

**Contraindications**

Hypersensitivity to ibuprofen; history of asthma, urticaria, or allergic-type reaction to aspirin or other NSAIDs; aspirin triad (eg, bronchial asthma, aspirin intolerance, rhinitis); perioperative pain in the setting of coronary artery bypass graft (CABG) surgery

Ibuprofen lysine (NeoProfen®): Preterm infants with untreated proven or suspected infection; congenital heart disease where patency of the PDA is necessary for pulmonary or systemic blood flow; bleeding (especially with active intracranial hemorrhage or GI bleed); thrombocytopenia; coagulation defects; proven or suspected necrotizing enterocolitis (NEC); significant renal dysfunction

**Warnings/Precautions**

**Boxed warnings:**

- Cardiovascular events: See "Concerns related to adverse effects" below.
- Coronary artery bypass graft surgery: See "Disease-related concerns" below.

- Gastrointestinal events: See "Concerns related to adverse effects" below.

**Concerns related to adverse effects:**

- Anaphylactoid reactions: Even in patients without prior exposure anaphylactoid reactions may occur; patients with "aspirin triad" (bronchial asthma, aspirin intolerance, rhinitis) may be at increased risk. Do not use in patients who experience bronchospasm, asthma, rhinitis, or urticaria with NSAID or aspirin therapy.
- Cardiovascular events: **[U.S. Boxed Warning]: NSAIDs are associated with an increased risk of adverse cardiovascular thrombotic events, including fatal MI and stroke.** Risk may be increased with duration of use or pre-existing cardiovascular risk factors or disease. Carefully evaluate individual cardiovascular risk profiles prior to prescribing. Use caution with fluid retention. Avoid use in heart failure. Concurrent administration of ibuprofen, and potentially other nonselective NSAIDs, may interfere with aspirin's cardioprotective effect. Use the lowest effective dose for the shortest duration of time, consistent with individual patient goals, to reduce risk of cardiovascular events; alternate therapies should be considered for patients at high risk.
- CNS effects: May cause drowsiness, dizziness, blurred vision, and other neurologic effects which may impair physical or mental abilities; patients must be cautioned about performing tasks which require mental alertness (eg, operating machinery or driving). Discontinue use with blurred or diminished vision and perform ophthalmologic exam. Periodically evaluate vision in all patients receiving long-term therapy.
- Gastrointestinal events: **[U.S. Boxed Warning]: NSAIDs may increase risk of gastrointestinal irritation, inflammation, ulceration, bleeding, and perforation.** These events can be fatal and may occur at any time during therapy and without warning. Use caution with a history of GI disease (bleeding or ulcers), concurrent therapy with aspirin, anticoagulants and/or corticosteroids, smoking, use of ethanol, the elderly or debilitated patients. Use the lowest effective dose for the shortest duration of time, consistent with individual patient goals, to reduce risk of GI adverse events; alternate therapies should be considered for patients at high risk. When used concomitantly with 325 mg of aspirin, a substantial increase in the risk of gastrointestinal complications (eg, ulcer) occurs; concomitant gastroprotective therapy (eg, proton pump inhibitors) is recommended (Bhatt, 2008).
- Hematologic effects: Platelet adhesion and aggregation may be decreased; may prolong bleeding time; patients with coagulation disorders or who are receiving anticoagulants should be monitored closely. Anemia may occur; patients on long-term NSAID therapy should be monitored for anemia. Rarely, NSAID use has been associated with potentially severe blood dyscrasias (eg, agranulocytosis, thrombocytopenia, aplastic anemia).
- Hyperkalemia: NSAID use may increase the risk of hyperkalemia, particularly in the elderly, diabetics, renal disease, and with concomitant use of other agents capable of inducing hyperkalemia (eg, ACE-inhibitors). Monitor potassium closely.
- Ophthalmic events: Blurred/diminished vision, scotomata, and changes in color vision have been reported. Discontinue therapy and refer for ophthalmologic evaluation if symptoms occur.
- Skin reactions: NSAIDs may cause serious skin adverse events including exfoliative dermatitis, Stevens-Johnson syndrome (SJS), and toxic epidermal necrolysis (TEN); discontinue use at first sign of skin rash or hypersensitivity.

**Disease-related concerns:**

- Aseptic meningitis: May increase the risk of aseptic meningitis, especially in patients with systemic lupus erythematosus (SLE) and mixed connective tissue disorders.

- Asthma: Do not administer to patients with aspirin-sensitive asthma; severe bronchospasm may occur. Use caution in patients with other forms of asthma.
- Coronary artery bypass graft surgery: **[U.S. Boxed Warning]: Use is contraindicated for treatment of perioperative pain in the setting of coronary artery bypass graft (CABG) surgery.** Risk of MI and stroke may be increased with use following CABG surgery.
- Hepatic impairment: Use with caution in patients with decreased hepatic function. Closely monitor patients with any abnormal LFT. Severe hepatic reactions (eg, fulminant hepatitis, liver failure) have occurred with NSAID use, rarely; discontinue if signs or symptoms of liver disease develop, or if systemic manifestations occur.
- Hypertension: Use with caution; may cause new-onset hypertension or worsening of existing hypertension. Response to ACE inhibitors, thiazides, or loop diuretics may be impaired with concurrent use of NSAIDs.
- Renal impairment: NSAID use may compromise existing renal function; dose-dependent decreases in prostaglandin synthesis may result from NSAID use, reducing renal blood flow which may cause renal decompensation. Patients with impaired renal function, dehydration, heart failure, liver dysfunction, those taking diuretics, and ACE inhibitors, and the elderly are at greater risk of renal toxicity. Rehydrate patient before starting therapy; monitor renal function closely. Not recommended for use in patients with advanced renal disease. Long-term NSAID use may result in renal papillary necrosis.

**Special populations:**

- Elderly: The elderly are at increased risk for adverse effects (especially serious gastrointestinal events, CNS effects, renal toxicity) from NSAIDs even at low doses.

**Dosage form specific issues:**

- Ibuprofen injection (Caldolor™): Must be diluted prior to administration; hemolysis can occur if not diluted.
- Ibuprofen lysine injection (NeoProfen®): Hold second or third doses if urinary output is <0.6 mL/kg/hour. May alter signs of infection. May inhibit platelet aggregation; monitor for signs of bleeding. May displace bilirubin; use caution when total bilirubin is elevated. Long-term evaluations of neurodevelopment, growth, or diseases associated with prematurity following treatment have not been conducted. A second course of treatment, alternative pharmacologic therapy or surgery may be needed if the ductus arteriosus fails to close or reopens following the initial course of therapy. Avoid extravasation.
- Phenylalanine: Some products may contain phenylalanine.

**Other warnings/precautions:**

- Self medication (OTC use): Prior to self-medication, patients should contact healthcare provider if they have had recurring stomach pain or upset, ulcers, bleeding problems, high blood pressure, heart or kidney disease, other serious medical problems, are currently taking a diuretic, aspirin, anticoagulant, or are ≥60 years of age. If patients are using for migraines, they should also contact healthcare provider if they have not had a migraine diagnosis by healthcare provider, a headache that is different from usual migraine, worst headache of life, fever and neck stiffness, headache from head injury or coughing, first headache at ≥50 years of age, daily headache, or migraine requiring bed rest. Recommended dosages should not be exceeded, due to an increased risk of GI bleeding. Stop use and consult a healthcare provider if symptoms get worse, newly appear, fever lasts for >3 days or pain lasts >3 days (children) and >10 days (adults). Do not give for >10 days unless instructed by healthcare provider. Consuming ≥3 alcoholic beverages/day or taking longer than recommended may increase the risk of GI bleeding.

• Surgical/dental procedures: Withhold for at least 4-6 half-lives prior to surgical or dental procedures.

**Adverse Reactions**

**Oral:**

1% to 10%:

Cardiovascular: Edema (1% to 3%)

Central nervous system: Dizziness (3% to 9%), headache (1% to 3%), nervousness (1% to 3%)

Dermatologic: Rash (3% to 9%), itching (1% to 3%)

Endocrine & metabolic: Fluid retention (1% to 3%)

Gastrointestinal: Epigastric pain (3% to 9%), heartburn (3% to 9%), nausea (3% to 9%), abdominal pain/cramps/distress (1% to 3%), appetite decreased (1% to 3%), constipation (1% to 3%), diarrhea (1% to 3%), dyspepsia (1% to 3%), flatulence (1% to 3%), vomiting (1% to 3%)

Otic: Tinnitus (3% to 9%)

<1%: Acute renal failure, agranulocytosis, allergic rhinitis, alopecia, amblyopia, anaphylaxis, arrhythmia, aplastic anemia, aseptic meningitis, azotemia, blurred vision, bone marrow suppression, bronchospasm, CHF, confusion, conjunctivitis, creatinine clearance decreased, cystitis, depression, drowsiness, dry eyes, duodenal ulcer, edema, emotional lability, eosinophilia, epistaxis, erythema multiforme, gastric ulcer, gastritis, GI bleed, GI hemorrhage, GI ulceration, hallucinations, hearing decreased, hematuria, hematocrit decreased, hemoglobin decreased, hemolytic anemia, hepatitis, hypertension, inhibition of platelet aggregation, insomnia, jaundice, liver function tests abnormal, leukopenia, melena, neutropenia, palpitation, pancreatitis, peripheral neuropathy, photosensitivity, polydipsia, polyuria, Stevens-Johnson syndrome, tachycardia, thrombocytopenia, toxic amblyopia, toxic epidermal necrolysis, urticaria, vesiculobullous eruptions, vision changes

**Injection: Ibuprofen (Caldolor™):** Abdominal pain, anemia, BUN increased, cough, dizziness, dyspepsia, edema, flatulence, headache, hemorrhage, hypokalemia, hypernatremia, hypertension, nausea, neutropenia, pruritis, urinary retention, vomiting

**Injection: Ibuprofen lysine (NeoProfen®):**

>10%:

Cardiovascular: Intraventricular hemorrhage (29%; grade 3/4: 15%)

Dermatologic: Skin irritation (16%)

Endocrine & metabolic: Hypocalcemia (12%), hypoglycemia (12%)

Gastrointestinal: GI disorders, non NEC (22%)

Hematologic: Anemia (32%)

Respiratory: Apnea (28%), respiratory infection (19%)

Miscellaneous: Sepsis (43%)

1% to 10%:

Cardiovascular: Edema (4%)

Endocrine & metabolic: Adrenal insufficiency (7%), hypernatremia (7%)

Genitourinary: Urinary tract infection (9%)

Renal: Urea increased (7%), renal impairment (6%), creatinine increased (3%), urine output decreased (3%; small decrease reported on days 2-6 with compensatory increase in output on day 9), renal failure (1%)

Respiratory: Respiratory failure (10%), atelectasis (4%)

Frequency not defined: Abdominal distension, cholestasis, feeding problems, gastritis, GI reflux, heart failure, hyperglycemia, hypotension, ileus, infection, inguinal hernia, injection site reaction, jaundice, neutropenia, seizure, tachycardia, thrombocytopenia

Postmarketing and/or case reports: GI perforation, necrotizing enterocolitis

### Metabolism/Transport Effects

**Substrate** (minor) of CYP2C9, 2C19; **Inhibits** CYP2C9 (strong)

### Drug Interactions

ACE Inhibitors: Nonsteroidal Anti-Inflammatory Agents may diminish the antihypertensive effect of ACE Inhibitors. *Risk C: Monitor therapy*

Aminoglycosides: Nonsteroidal Anti-Inflammatory Agents may decrease the excretion of Aminoglycosides. Data only in premature infants. *Risk C: Monitor therapy*

Angiotensin II Receptor Blockers: Nonsteroidal Anti-Inflammatory Agents may diminish the therapeutic effect of Angiotensin II Receptor Blockers. The combination of these two agents may also significantly decrease glomerular filtration and renal function. *Risk C: Monitor therapy*

Anticoagulants: Antiplatelet Agents may enhance the anticoagulant effect of Anticoagulants. *Risk C: Monitor therapy*

Anticoagulants: Nonsteroidal Anti-Inflammatory Agents may enhance the anticoagulant effect of Anticoagulants. *Risk C: Monitor therapy*

Antidepressants (Tricyclic, Tertiary Amine): May enhance the antiplatelet effect of NSAID (Nonselective). *Risk C: Monitor therapy*

Antiplatelet Agents: May enhance the anticoagulant effect of other Antiplatelet Agents. *Risk C: Monitor therapy*

Antiplatelet Agents: Nonsteroidal Anti-Inflammatory Agents may enhance the adverse/toxic effect of Antiplatelet Agents. An increased risk of bleeding may occur. Nonsteroidal Anti-Inflammatory Agents may diminish the cardioprotective effect of Antiplatelet Agents. This interaction is likely specific to aspirin, and not to other antiplatelet agents. *Risk C: Monitor therapy*

Beta-Blockers: Nonsteroidal Anti-Inflammatory Agents may diminish the antihypertensive effect of Beta-Blockers. **Exceptions:** Levobunolol; Metipranolol. *Risk C: Monitor therapy*

Bile Acid Sequestrants: May decrease the absorption of Nonsteroidal Anti-Inflammatory Agents. *Risk D: Consider therapy modification*

Bisphosphonate Derivatives: Nonsteroidal Anti-Inflammatory Agents may enhance the adverse/toxic effect of Bisphosphonate Derivatives. Both an increased risk of gastrointestinal

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- ulceration and an increased risk of nephrotoxicity are of concern. *Risk C: Monitor therapy*
  
- Carvedilol: CYP2C9 Inhibitors (Strong) may increase the serum concentration of Carvedilol. Specifically, concentrations of the S-carvedilol enantiomer may be increased. *Risk C: Monitor therapy*
  
- Corticosteroids (Systemic): May enhance the adverse/toxic effect of NSAID (Nonselective). *Risk C: Monitor therapy*
  
- CycloSPORINE: Nonsteroidal Anti-Inflammatory Agents may enhance the nephrotoxic effect of CycloSPORINE. Nonsteroidal Anti-Inflammatory Agents may increase the serum concentration of CycloSPORINE. *Risk D: Consider therapy modification*
  
- CycloSPORINE, Systemic: Nonsteroidal Anti-Inflammatory Agents may enhance the nephrotoxic effect of CycloSPORINE, Systemic. Nonsteroidal Anti-Inflammatory Agents may increase the serum concentration of CycloSPORINE, Systemic. *Risk D: Consider therapy modification*
  
- CYP2C9 Substrates (High risk): CYP2C9 Inhibitors (Strong) may decrease the metabolism of CYP2C9 Substrates (High risk). *Risk D: Consider therapy modification*
  
- Dasatinib: May enhance the anticoagulant effect of Antiplatelet Agents. *Risk C: Monitor therapy*
  
- Desmopressin: Nonsteroidal Anti-Inflammatory Agents may enhance the adverse/toxic effect of Desmopressin. *Risk C: Monitor therapy*
  
- Drotrecogin Alfa: Antiplatelet Agents may enhance the adverse/toxic effect of Drotrecogin Alfa. Bleeding may occur. *Risk D: Consider therapy modification*
  
- Eplerenone: Nonsteroidal Anti-Inflammatory Agents may diminish the antihypertensive effect of Eplerenone. Nonsteroidal Anti-Inflammatory Agents may enhance the hyperkalemic effect of Eplerenone. *Risk C: Monitor therapy*
  
- Glucosamine: May enhance the antiplatelet effect of Antiplatelet Agents. *Risk C: Monitor therapy*
  
- Herbs (Anticoagulant/Antiplatelet Properties) (eg, Alfalfa, Anise, Bilberry): May enhance the adverse/toxic effect of Antiplatelet Agents. Bleeding may occur. *Risk D: Consider therapy modification*
  
- Herbs (Anticoagulant/Antiplatelet Properties) (eg, Alfalfa, Anise, Bilberry): May enhance the adverse/toxic effect of Nonsteroidal Anti-Inflammatory Agents. Bleeding may occur. *Risk D: Consider therapy modification*
  
- HydrALAZINE: Nonsteroidal Anti-Inflammatory Agents may diminish the antihypertensive effect of HydrALAZINE. *Risk C: Monitor therapy*
  
- Ibritumomab: Antiplatelet Agents may enhance the adverse/toxic effect of Ibritumomab. Both agents may contribute to impaired platelet function and an increased risk of bleeding. *Risk C: Monitor therapy*
  
- Ketorolac: May enhance the adverse/toxic effect of Nonsteroidal Anti-Inflammatory Agents. *Risk X: Avoid combination*
  
- Ketorolac, Systemic: May enhance the adverse/toxic effect of Nonsteroidal Anti-Inflammatory Agents. *Risk X: Avoid combination*
  
- Lithium: Nonsteroidal Anti-Inflammatory Agents may increase the serum concentration of

Lithium. *Risk D: Consider therapy modification*

Loop Diuretics: Nonsteroidal Anti-Inflammatory Agents may diminish the diuretic effect of Loop Diuretics. *Risk C: Monitor therapy*

Methotrexate: Nonsteroidal Anti-Inflammatory Agents may decrease the excretion of Methotrexate. *Risk D: Consider therapy modification*

Nonsteroidal Anti-Inflammatory Agents: May enhance the adverse/toxic effect of Antiplatelet Agents. An increased risk of bleeding may occur. Nonsteroidal Anti-Inflammatory Agents may diminish the cardioprotective effect of Antiplatelet Agents. This interaction is likely specific to aspirin, and not to other antiplatelet agents. *Risk C: Monitor therapy*

Nonsteroidal Anti-Inflammatory Agents: May enhance the adverse/toxic effect of other Nonsteroidal Anti-Inflammatory Agents. *Risk C: Monitor therapy*

Omega-3-Acid Ethyl Esters: May enhance the antiplatelet effect of Antiplatelet Agents. *Risk C: Monitor therapy*

Pemetrexed: NSAID (Nonselective) may increase the serum concentration of Pemetrexed. Management: Patients with mild-to-moderate renal insufficiency (CrCl 45-79 mL/minute) may use ibuprofen with caution, but should avoid other NSAIDs for 2-5 days prior to, the day of, and 2 days after pemetrexed. *Risk D: Consider therapy modification*

Pentosan Polysulfate Sodium: May enhance the adverse/toxic effect of Antiplatelet Agents. Specifically, the risk of bleeding may be increased by concurrent use of these agents. *Risk C: Monitor therapy*

Pentoxifylline: May enhance the antiplatelet effect of Antiplatelet Agents. *Risk C: Monitor therapy*

Potassium-Sparing Diuretics: Nonsteroidal Anti-Inflammatory Agents may diminish the antihypertensive effect of Potassium-Sparing Diuretics. Nonsteroidal Anti-Inflammatory Agents may enhance the hyperkalemic effect of Potassium-Sparing Diuretics. *Risk C: Monitor therapy*

Pralatrexate: Nonsteroidal Anti-Inflammatory Agents may increase the serum concentration of Pralatrexate. More specifically, NSAIDs may decrease the renal excretion of pralatrexate. Management: Closely monitor for increased pralatrexate serum levels and/or toxicity if used concomitantly with an NSAID. Monitor for decreased pralatrexate serum levels with NSAID discontinuation. *Risk C: Monitor therapy*

Probenecid: May increase the serum concentration of Nonsteroidal Anti-Inflammatory Agents. *Risk C: Monitor therapy*

Prostacyclin Analogues: May enhance the antiplatelet effect of Antiplatelet Agents. *Risk C: Monitor therapy*

Quinolone Antibiotics: Nonsteroidal Anti-Inflammatory Agents may enhance the neuroexcitatory and/or seizure-potentiating effect of Quinolone Antibiotics. *Risk C: Monitor therapy*

Salicylates: NSAID (Nonselective) may enhance the adverse/toxic effect of Salicylates. An increased risk of bleeding may be associated with use of this combination. NSAID (Nonselective) may diminish the cardioprotective effect of Salicylates. Salicylates may decrease the serum concentration of NSAID (Nonselective). **Exceptions:** Choline Magnesium Trisalicylate. *Risk D: Consider therapy modification*

Salicylates: Antiplatelet Agents may enhance the adverse/toxic effect of Salicylates.

Increased risk of bleeding may result. *Risk C: Monitor therapy*

Selective Serotonin Reuptake Inhibitors: May enhance the antiplatelet effect of NSAID (Nonselective). *Risk D: Consider therapy modification*

Serotonin/Norepinephrine Reuptake Inhibitors: May enhance the antiplatelet effect of NSAID (Nonselective). *Risk C: Monitor therapy*

Thiazide Diuretics: Nonsteroidal Anti-Inflammatory Agents may diminish the therapeutic effect of Thiazide Diuretics. *Risk C: Monitor therapy*

Thrombolytic Agents: Antiplatelet Agents may enhance the anticoagulant effect of Thrombolytic Agents. *Risk C: Monitor therapy*

Thrombolytic Agents: Nonsteroidal Anti-Inflammatory Agents may enhance the adverse/toxic effect of Thrombolytic Agents. An increased risk of bleeding may occur. *Risk C: Monitor therapy*

Tositumomab and Iodine I 131 Tositumomab: Antiplatelet Agents may enhance the adverse/toxic effect of Tositumomab and Iodine I 131 Tositumomab. Specifically, the risk of bleeding-related adverse events may be increased. *Risk C: Monitor therapy*

Treprostinil: May enhance the adverse/toxic effect of Nonsteroidal Anti-Inflammatory Agents. Bleeding may occur. *Risk C: Monitor therapy*

Vancomycin: Nonsteroidal Anti-Inflammatory Agents may decrease the excretion of Vancomycin. *Risk C: Monitor therapy*

Vitamin K Antagonists (eg, warfarin): NSAID (Nonselective) may enhance the anticoagulant effect of Vitamin K Antagonists. *Risk D: Consider therapy modification*

### **Ethanol/Nutrition/Herb Interactions**

Ethanol: Avoid ethanol (may enhance gastric mucosal irritation).

Food: Ibuprofen peak serum levels may be decreased if taken with food.

Herb/Nutraceutical: Avoid alfalfa, anise, bilberry, bladderwrack, bromelain, cat's claw, celery, chamomile, coleus, cordyceps, dong quai, evening primrose, fenugreek, feverfew, garlic, ginger, ginkgo biloba, ginseng (American, Panax, Siberian), grapeseed, green tea, guggul, horse chestnut seed, horseradish, licorice, prickly ash, red clover, reishi, SAME (S-adenosylmethionine), sweet clover, turmeric, white willow (all have additional antiplatelet activity).

### **Storage**

Ibuprofen injection (Caldolor™): Store intact vials at room temperature of 20°C to 25°C (68°F to 77°F). Must be diluted prior to use. Diluted solutions stable for 24 hours at room temperature.

Ibuprofen lysine injection (NeoProfen®): Store at room temperature of 20°C to 25°C (68°F to 77°F). Protect from light. Following dilution, administer within 30 minutes of preparation.

### **Reconstitution**

Ibuprofen injection (Caldolor™): Must be diluted prior to use. Dilute with D<sub>5</sub>W, NS or LR to a final concentration ?4 mg/mL.

Ibuprofen lysine injection (NeoProfen®): Dilute with dextrose or saline to an appropriate volume.

### **Compatibility**

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Ibuprofen injection (Caldolor™): Stable in dextrose, saline, and lactated Ringer's

Ibuprofen lysine injection (NeoProfen®): Stable in dextrose, saline; **incompatible** with TPN solution.

**Mechanism of Action**

Reversibly inhibits cyclooxygenase-1 and 2 (COX-1 and 2) enzymes, which results in decreased formation of prostaglandin precursors; has antipyretic, analgesic, and anti-inflammatory properties

Other proposed mechanisms not fully elucidated (and possibly contributing to the anti-inflammatory effect to varying degrees), include inhibiting chemotaxis, altering lymphocyte activity, inhibiting neutrophil aggregation/activation, and decreasing proinflammatory cytokine levels.

**Pharmacodynamics/Kinetics**

Onset of action: Oral: Analgesic: 30-60 minutes; Anti-inflammatory: ?7 days

Peak effect: Oral: 1-2 weeks

Duration: Oral: 4-6 hours

Absorption: Oral: Rapid (85%)

Distribution: V<sub>d</sub>: 6.35 L; premature infants with ductal closure (highly variable between studies):

Day 3: 145-349 mL/kg

Day 5: 72-222 mL/kg

Protein binding: 90% to 99%

Metabolism: Hepatic via oxidation

Half-life elimination:

Premature infants (highly variable between studies):

Day 3: 35-51 hours

Day 5: 20-33 hours

Children 3 months to 10 years: 1.6 ± 0.7 hours

Adults: 2-4 hours; End-stage renal disease: Unchanged

Time to peak: Oral: ~1-2 hours

Excretion: Urine (primarily as metabolites; 1% as unchanged drug); some feces

**Dosage**

I.V.:

Neonates: Ibuprofen lysine (NeoProfen®): Infants between 500-1500 g and ?32 weeks GA: Patent ductus arteriosus: Initial dose: Ibuprofen 10 mg/kg, followed by two doses of 5 mg/kg at 24 and 48 hours. Dose should be based on birth weight.

Adults (Caldolor™): **Note:** Patients should be well hydrated prior to administration

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Analgesic: 400-800 mg every 6 hours as needed (maximum: 3.2 g/day)

Antipyretic: Initial: 400 mg, then every 4-6 hours or 100-200 mg every 4 hours as needed (maximum: 3.2 g/day)

Oral:

Children:

Antipyretic: 6 months to 12 years: Temperature <102.5°F (39°C): 5 mg/kg/dose; temperature >102.5°F: 10 mg/kg/dose given every 6-8 hours (maximum daily dose: 40 mg/kg/day)

Juvenile rheumatoid arthritis: 30-50 mg/kg/24 hours divided every 8 hours; start at lower end of dosing range and titrate upward (maximum: 2.4 g/day)

Analgesic: 4-10 mg/kg/dose every 6-8 hours

Cystic fibrosis (unlabeled use): Chronic (>4 years) twice daily dosing adjusted to maintain serum concentration of 50-100 mcg/mL has been associated with slowing of disease progression in younger patients with mild lung disease

OTC labeling (analgesic, antipyretic): **Note:** Treatment for >10 days is not recommended unless directed by healthcare provider.

Children 6 months to 11 years: See table; use of weight to select dose is preferred; doses may be repeated every 6-8 hours (maximum: 4 doses/day)

Children ?12 years: 200 mg every 4-6 hours as needed (maximum: 1200 mg/24 hours)

Ibuprofen Dosing Weight (lb) Age Dosage (mg)  
12-17 6-11 mo 50 18-23 12-23 mo 75 24-35 2-3 y 100 36-47 4-5 y 150 48-59 6-8 y 200 60-71 9-10 y 250 72-95 11 y 300  
Table has been converted to the following text. Ibuprofen Dosing Weight 12-17 lbs (6-11 months of age): 50 mg Weight 18-23 lbs (12-23 months of age): 75 mg Weight 24-35 lbs (2-3 years of age): 100 mg Weight 36-47 lbs (4-5 years of age): 150 mg Weight 48-59 lbs (6-8 years of age): 200 mg Weight 60-71 lbs (9-10 years of age): 250 mg Weight 72-95 lbs (11 years of age): 300 mg

Adults:

Inflammatory disease: 400-800 mg/dose 3-4 times/day (maximum dose: 3.2 g/day)

Analgesia/pain/fever/dysmenorrhea: 200-400 mg/dose every 4-6 hours (maximum daily dose: 1.2 g, unless directed by physician; under physician supervision daily doses ?2.4 g may be used)

OTC labeling (analgesic, antipyretic): 200 mg every 4-6 hours as needed (maximum: 1200 mg/24 hours); treatment for >10 days is not recommended unless directed by healthcare provider.

Migraine: 2 capsules at onset of symptoms (maximum: 400 mg/24 hours unless directed by healthcare provider)

**Dosing adjustment/comments in renal impairment:** If anuria or oliguria evident, hold dose until renal function returns to normal

**Dosing adjustment/comments in severe hepatic impairment:** Avoid use

**Dental Usual Dosing**

Analgesic/pain/fever/dysmenorrhea: Oral:

Children: 4-10 mg/kg/dose every 6-8 hours

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Adults: 200-400 mg/dose every 4-6 hours (maximum daily dose: 1.2 g, unless directed by physician; under physician supervision daily doses ?2.4 g may be used)

OTC labeling (analgesic, antipyretic): **Note:** Treatment for >10 days is not recommended unless directed by healthcare provider. Oral:

Children 6 months to 11 years: See table; use of weight to select dose is preferred; doses may be repeated every 6-8 hours (maximum: 4 doses/day)

Children ?12 years and Adults: 200 mg every 4-6 hours as needed (maximum: 1200 mg/24 hours)

Ibuprofen Dosing Weight (lb) Age Dosage (mg) 12-17 6-11 mo 50 18-23 12-23 mo 75 24-35 2-3 y 100 36-47 4-5 y 150 48-59 6-8 y 200 60-71 9-10 y 250 72-95 11 y 300 Table has been converted to the following text. Ibuprofen Dosing Weight 12-17 lbs (6-11 months of age): 50 mg Weight 18-23 lbs (12-23 months of age): 75 mg Weight 24-35 lbs (2-3 years of age): 100 mg Weight 36-47 lbs (4-5 years of age): 150 mg Weight 48-59 lbs (6-8 years of age): 200 mg Weight 60-71 lbs (9-10 years of age): 250 mg Weight 72-95 lbs (11 years of age): 300 mg

**Administration: Oral**

Administer with food.

**Administration: I.V.**

Caldolor™: For I.V. administration only; must be diluted to a final concentration of ?4 mg/mL prior to administration; infuse over at least 30 minutes

NeoProfen® (ibuprofen lysine): For I.V. administration only; administration via umbilical arterial line has not been evaluated. Infuse over 15 minutes through port closest to insertion site. Avoid extravasation. Do not administer simultaneously via same line with TPN. If needed, interrupt TPN for 15 minutes prior to and after ibuprofen administration, keeping line open with dextrose or saline.

**Administration: I.V. Detail**

Caldolor™: pH: 7.4

NeoProfen®: pH: 7.0

**Monitoring Parameters**

CBC, chemistry profile, occult blood loss and periodic liver function tests; monitor response (pain, range of motion, grip strength, mobility, ADL function), inflammation; observe for weight gain, edema; monitor renal function (urine output, serum BUN and creatinine); observe for bleeding, bruising; evaluate gastrointestinal effects (abdominal pain, bleeding, dyspepsia); mental confusion, disorientation; with long-term therapy, periodic ophthalmic exams; signs of infection (ibuprofen lysine)

**Reference Range**

Plasma concentrations >200 mcg/mL may be associated with severe toxicity

PDA: Minimum effective concentration: 10-12 mg/L

**Dietary Considerations**

Should be taken with food. Some products may contain phenylalanine.

**Patient Education**

If self-administered, use exactly as directed; do not increase dose or frequency. Adverse reactions can occur with overuse. Consult your prescriber before use if you have hypertension or heart failure. Do not take longer than 3 days for fever, or 10 days for pain without consulting medical advisor. Take with food or milk. While using this medication, do not use alcohol, excessive amounts of vitamin C, or salicylate-containing foods (curry powder,

prunes, raisins, tea, or licorice), other prescription or OTC medications containing aspirin or salicylate, or other NSAIDs without consulting prescriber. Maintain adequate hydration unless instructed to restrict fluid intake. You may experience nausea, vomiting, gastric discomfort (frequent mouth care, small frequent meals, chewing gum, sucking lozenges may help). GI bleeding, ulceration, or perforation can occur with or without pain. Stop taking medication and report ringing in ears; persistent cramping or stomach pain; unresolved nausea or vomiting; respiratory difficulty or shortness of breath; unusual bruising or bleeding (mouth, urine, stool); skin rash; unusual swelling of extremities; chest pain; or palpitations. **Pregnancy/breast-feeding precautions:** Inform prescriber if you are or intend to become pregnant. This drug should not be used in the 3rd trimester of pregnancy. Consult prescriber if breast-feeding.

#### **Geriatric Considerations**

Elderly are a high-risk population for adverse effects from NSAIDs. As much as 60% of elderly can develop peptic ulceration and/or hemorrhage asymptotically. The concomitant use of H<sub>2</sub> blockers and sucralfate is not effective as prophylaxis with the exception of NSAID-induced duodenal ulcers which may be prevented by the use of ranitidine. Misoprostol and proton pump inhibitors are the only agents proven to help prevent the development of NSAID-induced ulcers. Also, concomitant disease and drug use contribute to the risk for GI adverse effects. Use lowest effective dose for shortest period possible. Consider renal function decline with age. Use of NSAIDs can compromise existing renal function especially when Cl<sub>Cr</sub> is  $\leq 30$  mL/minute. Tinnitus may be a difficult and unreliable indication of toxicity due to age-related hearing loss or eighth cranial nerve damage. CNS adverse effects such as confusion, agitation, and hallucination are generally seen in overdose or high dose situations, but the elderly may demonstrate these adverse effects at lower doses than younger adults.

#### **Anesthesia and Critical Care Concerns/Other Considerations**

The 2002 ACCM/SCCM guidelines for analgesia (critically-ill adult) suggest that NSAIDs may be used in combination with opioids in select patients for pain management. Concern about adverse events (increased risk of renal dysfunction, altered platelet function and gastrointestinal irritation) limits its use in patients who have other underlying risks for these events.

In short-term use, NSAIDs vary considerably in their effect on blood pressure. When NSAIDs are used in patients with hypertension, monitor blood pressure response, and duration of therapy, when possible, should be kept short. The use of NSAIDs in the treatment of patients with heart failure may be associated with an increased risk for fluid accumulation and edema; may precipitate renal failure in dehydrated patients by inhibition of prostaglandin-mediated autoregulation. Use extreme caution or avoid concurrent use with nephrotoxic agents.

#### **Cardiovascular Considerations**

**Blood Pressure:** In short-term use, NSAIDs vary considerably in their effect on blood pressure. A meta-analysis (Pope, 1993) showed that indomethacin and naproxen had the largest effect on blood pressure. Other NSAIDs, including piroxicam, ibuprofen, and sulindac had less of an effect. Ibuprofen combined with captopril or losartan may attenuate the antihypertensive effects of ACE inhibition or receptor blockade on sitting or 24-hour ambulatory diastolic blood pressure. When NSAIDs are used in patients with hypertension, appropriate monitoring of blood pressure responses should be completed and the duration of therapy, when possible, kept short.

**Heart Failure:** The use of NSAIDs in the treatment of patients with heart failure may be associated with an increased risk for fluid accumulation and edema. One study showed that NSAID use in elderly patients had an increased risk of hospitalization for heart failure. This study gives compelling reasons to avoid or limit the use of NSAIDs in patients with heart failure, particularly in the elderly population. The ACC/AHA 2009 heart failure guidelines suggest that NSAIDs be avoided or withdrawn whenever possible in patients with current or prior symptoms of heart failure and reduced LVEF.

**Risk of Cardiovascular Events:** Patients at increased risk of cardiovascular adverse events

include patients immediately postoperative (10-14 days) from CABG surgery, and those with existing CAD, CVD, or history of TIA. Prescribers are encouraged to use the lowest effective dose for the shortest duration of time based on individual patient treatment goals. Available evidence reviewed by the FDA does not suggest an increased risk of serious CV events when NSAIDs are given short term and in the lower doses used OTC.

**Drug Interactions:** Nonsteroidal anti-inflammatory agents, including ibuprofen and naproxen, may diminish the cardioprotective effect of aspirin (Catella-Lawson F, 2001; Capone ML, 2005). It is surmised that ibuprofen may exhibit greater affinity than aspirin for the COX-1 site or if dosed regularly (or prior to aspirin), it would gain access to the active site first. In either case, aspirin's inhibition of COX (irreversible) would be limited in favor of ibuprofen inhibition (reversible). Avoid regular use of NSAIDs (nonselective) if possible. If used occasionally, take 1/2 -2 hours after aspirin (immediate release) ingestion.

**Dental Health: Effects on Dental Treatment**

In a statement released on September 8, 2006, the FDA notified consumers and healthcare professionals that the administration of ibuprofen for pain relief to patients taking aspirin for cardioprotection may interfere with aspirin's cardiovascular benefits. The FDA states that ibuprofen can interfere with the antiplatelet effect of low-dose aspirin (81 mg/day). This could result in diminished effectiveness of aspirin as used for cardioprotection and stroke prevention. The FDA adds that although ibuprofen and aspirin can be taken together, it is recommended that consumers talk with their healthcare providers for additional information. For more information, including how to advise aspirin patients requiring ibuprofen for pain relief, see Effects on Bleeding and Dental Health Professional Considerations.

**Dental Health: Vasoconstrictor/Local Anesthetic Precautions**

No information available to require special precautions

**Dental Comment**

Preoperative use of ibuprofen at a dose of 400-600 mg every 6 hours 24 hours before the appointment decreases postoperative edema and hastens healing time.

New information from the FDA states that ibuprofen can interfere with the antiplatelet effect of low-dose aspirin (81 mg/day), potentially rendering aspirin less effective when used for cardioprotection and stroke protection. In situations where these drugs could be used concomitantly, the FDA has provided the following information.

Patients who use immediate release aspirin (not enteric-coated aspirin) and take a single dose or chronic doses of ibuprofen 400 mg, should dose the ibuprofen at least **30 minutes or longer after aspirin ingestion or more than 8 hours before aspirin ingestion** to avoid attenuation of aspirin's effect.

At this time, recommendations about the timing of ibuprofen 400 mg in patients taking enteric-coated low-dose aspirin cannot be made based on available data. One study however, showed that the antiplatelet effect of enteric-coated low-dose aspirin was attenuated when ibuprofen 400 mg was dosed 2, 7, and 12 hours after aspirin (Catella-Lawson, 2001).

With occasional use of ibuprofen, there is likely to be minimal risk from any attenuation of the antiplatelet effect of low-dose aspirin, because of a long-lasting effect of aspirin on platelets.

Other over-the-counter (OTC) NSAIDs (ie, naproxen sodium and ketoprofen) should be viewed as having the potential to interfere with the antiplatelet effect of low-dose aspirin until proven otherwise. However, the FDA is unaware of any studies that have looked at the same type of interference by ketoprofen with low-dose aspirin. One study of naproxen and low-dose aspirin has suggested that naproxen may interfere with aspirin's antiplatelet activity when they are coadministered (Steinhubl, 2005). However, naproxen 500 mg administered 2 hours before or after aspirin 100 mg, did not interfere with aspirin's antiplatelet effect. The FDA stated that there is no data looking at doses of naproxen <500 mg. Naproxen OTC strength is

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220 mg tablets.

**Mental Health: Effects on Mental Status**

Drowsiness and dizziness are common; may cause nervousness; may rarely cause insomnia, confusion, hallucinations, or depression

**Mental Health: Effects on Psychiatric Treatment**

May rarely cause agranulocytosis; use caution with clozapine and carbamazepine; may decrease lithium clearance resulting in an increase in serum lithium levels and potential lithium toxicity; monitor serum lithium levels

**Nursing: Physical Assessment/Monitoring**

Evaluate cardiac risk and potential for GI bleeding prior to prescribing this medication. Assess patient for allergic reaction to salicylates or other NSAIDs. Assess other medications patient may be taking for additive or adverse interactions. Monitor blood pressure at the beginning of therapy and periodically during use. Monitor therapeutic effectiveness and signs of adverse reactions or overdose at beginning of therapy and periodically during long-term therapy. With long-term therapy, periodic ophthalmic exams are recommended. Assess knowledge/teach patient appropriate use. Teach patient to monitor for adverse reactions, adverse reactions to report, and appropriate interventions to reduce side effects.

**Dosage Forms**

Excipient information presented when available (limited, particularly for generics); consult specific product labeling. [DSC] = Discontinued product

Caplet: 200 mg [OTC]

Advil®: 200 mg [contains sodium benzoate]

Ibu-200: 200 mg

Motrin® IB: 200 mg

Motrin® Junior: 100 mg [scored]

Capsule, liquid-filled:

Advil®: 200 mg [solubilized ibuprofen; contains potassium 20 mg]

Advil® Migraine: 200 mg [solubilized ibuprofen; contains potassium 20 mg]

Gelcap:

Advil®: 200 mg [contains coconut oil]

Injection, solution:

Caldolor™: 100 mg/mL (4 mL, 8 mL)

Injection, solution, as lysine [preservative free]:

NeoProfen®: 17.1 mg/mL (2 mL) [equivalent to ibuprofen 10 mg/mL]

Suspension, oral: 100 mg/5 mL (5 mL, 10 mL, 120 mL, 240 mL, 480 mL)

Advil® Children's: 100 mg/5 mL (120 mL) [contains sodium benzoate, sodium, propylene glycol; blue raspberry, fruit, and grape flavors]

Motrin® Children's: 100 mg/5 mL (60 mL, 120 mL) [contains sodium benzoate; berry, dye free berry, bubble gum, and grape flavors]

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Suspension, oral [concentrate, drops]: 40 mg/mL (15 mL)

Advil® Infants': 40 mg/mL (15 mL) [contains sodium benzoate; fruit, grape, and white grape flavors]

Motrin® Infants': 40 mg/mL (15 mL) [contains sodium benzoate; ethanol free; berry and dye-free berry flavors]

Tablet: 200 mg [OTC], 400 mg, 600 mg, 800 mg

Addaprin: 200 mg

Advil®: 200 mg [contains sodium benzoate]

Genpril®: 200 mg [DSC]

Ibu®: 400 mg, 600 mg, 800 mg

Ibu-200: 200 mg

I-Prin: 200 mg

Midol® Cramp and Body Aches: 200 mg

Motrin® IB: 200 mg

Propriinal: 200 mg [contains sodium benzoate]

Ultraprin: 200 mg [sugar free]

Tablet, chewable:

Advil® Children's: 50 mg [contains phenylalanine 2.1 mg; grape flavors]

Advil® Junior: 100 mg [contains phenylalanine 4.2 mg; grape flavors] [DSC]

Motrin® Junior: 100 mg [contains phenylalanine 2.1 mg; grape and orange flavors]

**Pricing: U.S. ([www.drugstore.com](http://www.drugstore.com))**

**Suspension** (Ibuprofen)

100 mg/5 mL (473): \$24.27

**Tablets** (Advil)

200 mg (100): \$18.99

**Tablets** (Ibuprofen)

400 mg (30): \$11.99

600 mg (90): \$14.99

800 mg (30): \$12.59

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#### International Brand Names

- Actron (PY, UY)
- Adex 200 (IL)
- Adex Liqui-Gels (IL)
- Advil (AU, BR, CO, CR, DO, EC, EE, ES, FR, GT, HN, IL, MX, NI, PA, PL, SV, VE, ZA)
- Algofen (IT)
- Am-Fam 400 (IN)
- Anafen (ID)
- Anco (DE)
- Antarene (FR)
- Balkaprofen (BF, BJ, CI, ET, GH, GM, GN, KE, LR, MA, ML, MR, MU, MW, NE, NG, SC, SD, SL, SN, TN, TZ, UG, ZA, ZM, ZW)
- Bestafen (MX)
- Bifen (HK, SG)
- Brufen (AE, AT, AU, BD, BE, BG, BH, CH, CL, CY, CZ, DE, DK, EG, ES, FI, FR, GB, GR, HK, HN, ID, IE, IL, IN, IQ, IR, IT, JO, JP, KP, KW, LB, LY, MY, NL, NO, NZ, OM, PH, PK, PL, PT, QA, RU, SA, SE, SG, SY, TH, TR, TW, YE, ZA)
- Brufen 400 (IL)
- Brufen Retard (NZ)
- Brufort (IT)
- Bufect (ID)
- Bufect Forte (ID)
- Burana (FI)
- Carol (KP)
- Cenbufen (TH)
- Codral Period Pain (AU)
- Cuprofen (TH)
- Degiton (TW)
- Diffutab SR 600 (KP)
- Dolafen (PH)
- Dolan FP (PH)
- Dolgit (AE, BH, CY, DE, EG, IL, IQ, IR, JO, KW, LB, LY, OM, QA, SA, SY, YE)
- Dolocyl (CH)
- Dolofen-F (ID)
- Dolomax (PE)
- Dolormin (DE)
- Drin (GR)
- Druisel (AR)
- Easifon (TW)
- Expanfen (FR)
- Febratic (MX)

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- Fenbid (AE, BF, BH, BJ, CI, CY, EG, ET, GB, GH, GM, GN, IL, IQ, IR, JO, KE, KW, LB, LR, LY, MA, ML, MR, MU, MW, NE, NG, OM, QA, SA, SC, SD, SL, SN, SY, TN, TZ, UG, YE, ZA, ZM, ZW)
- Fenpaed (NZ)
- Focus (IT)
- Gesica (TH)
- Gyno-neuralgin (DE)
- Ibufac (MY)
- Ibufen (IL)
- Ibuflam (MX)
- Ibufug (DE)
- Ibugesic (IN)
- Ibulgan (AE, BB, BF, BH, BJ, BM, BS, BZ, CI, CY, EG, ET, GH, GM, GN, GY, IL, IQ, IR, JM, JO, KE, KW, LB, LR, LY, MA, ML, MR, MU, MW, NE, NG, OM, QA, SA, SC, SD, SL, SN, SR, SY, TN, TT, TZ, UG, YE, ZA, ZM, ZW)
- Ibumetin (DK, FI, NL, NO, SE)
- Ibupirac (AR, CN)
- Ibuprofen (HK)
- Ibuprox (ES)
- Ibusal (FI)
- Idyl SR (PH)
- Infacalm (HK)
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- Iprox (ID)
- Ipufen (TW)
- Irfen (AE, BH, CH, CY, EG, IL, IQ, IR, JO, KW, LB, LY, OM, QA, SA, SY, YE)
- Liptan (AE, BH, CY, EG, IL, IQ, IR, JO, JP, KW, LB, LY, OM, QA, SA, SY, YE)
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- Motrin (AE, BH, CO, CR, CY, EC, EG, GT, HN, IL, IQ, IR, JO, KW, LB, LY, MX, NI, OM, PA, PE, QA, SA, SV, SY, TW, YE)
- Neutropain (HK)
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- Noritis (BF, BJ, CI, ET, GH, GM, GN, KE, LR, MA, ML, MR, MU, MW, NE, NG, SC, SD, SL, SN, TN, TZ, UG, ZA, ZM, ZW)
- Novogent (DE)
- Nurofen (AT, BE, BF, BG, BJ, CI, CZ, DK, ET, FR, GB, GH, GM, GN, KE, LR, MA, ML, MR, MU, MW, MY, NE, NG, NL, SC, SD, SE, SG, SL, SN, TN, TR, TZ, UG, ZA, ZM, ZW)
- Nurofen for Children (TH)
- Nurofen Gel (IL)
- Nurofen Pro san sucre (FR)
- Optifen (CH)
- Opturem (DE)
- Ostarin (ID)
- Panafen IB (AU)
- Pedea (AT, BE, BG, CH, CZ, DE, DK, ES, FI, FR, GB, GR, HN, IE, IT, NL, NO, PL, PT, RU, SE, TR)
- Perfen (TW)
- Perofen (BB, BM, BS, BZ, GY, JM, SR, TT)

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- Profen (HK, ID)
- Proris (ID)
- Prosinal (ID)
- Proven (AU)
- Provon (PE)
- Quadrax (MX)
- Rafen (AU)
- Ranofen (ZA)
- Rhelafen (ID)
- Rhelafen Forte (ID)
- Rupan (AE, BH, CY, EG, IL, IQ, IR, JO, KW, LB, LY, OM, QA, SA, SY, YE)
- Spedifen (FR)
- Speedifen (TH)
- Spifen (FR)
- Syntofene (FR)
- Tabalon 400 (MX)
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- Taskine (AE, BH, CY, EG, IL, IQ, IR, JO, KW, LB, LY, OM, QA, SA, SY, YE)
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